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**WO 2003/104762 A3**

(54) Title: PROTEIN MICRO-ARRAYS AND MULTI-LAYERED AFFINITY INTERACTION DETECTION

(57) Abstract: The present invention provides proteomic techniques that extend sensitive and quantitative analysis of proteins to post-translational modifications. Protein micro-arrays and/or multiplex coded-microbeads are used in combination with multilayered affinity interaction detection (MAID) methods that permit high throughput analysis of cellular protein modifications and functional protein interactions.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US02/33917

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : G01N 33/53

US CL : 435/7.1

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
EAST, MEDLINE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6,329,209 B1 (WAGNER et al) 11 December 2001 (11.12.2001), see all document	1, 4-11, 22-32
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Y		2, 3, 14-21
X	US 6,255,455 B1 (SIEGEL) 03 July 2001 (03.07.2001), see all document	1-3, 5-32
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Y		4
X	US 6,197,599 B1 (CHIN et al) 06 March 2001 (06.03.2001), see all document	1-32
Y	US 5,985,543 A (SIEGEL) 16 November 1999 (16.11.1999), see all document	1-32
Y	US 2001/0031469 A1 (VOLINIA) 18 October 2001 (18.10.2001), see all document	1-32
Y	US 5,268,305 A (RIBI et al) 07 December 1993 (07.12.1993), see all document	1-32
X, E	US 2003/0207467 A1 (SNYDER et al) 06 November 2003 (06.11.2003), see all document	1-32

Further documents are listed in the continuation of Box C.

See patent family annex.

Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"B" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

22 January 2004 (22.01.2004)

Date of mailing of the international search report

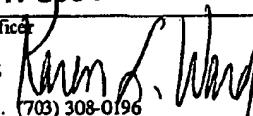
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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US02/33917

**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

 No protest accompanied the payment of additional search fees.

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-3, 5-21, drawn to a method of analyzing post-translational protein modifications in a sample comprising the special feature of binding proteins of a sample to a detectable affinity reagent and then applying the sample to an array of immobilized protein capture agents.

Group 2, claim(s) 1-, 4-11, drawn to a method of analyzing post-translational protein modifications in a sample comprising the special feature of applying the sample to an array of immobilized protein capture agents and then binding proteins of a sample to a detectable affinity reagent.

Group 3, claim(s) 22-32, drawn to a kit for a high throughput and quantitative method of analyzing post-translational protein modifications in a sample.

The inventions listed as Groups 1-3 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The application contains claims to more than one of the combinations of categories of inventions as set forth by 37 CFR 1.475.

According to 37 CFR 1.475 regarding unity of invention:

(a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

(b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

- (1) A product and a process specially adapted for the manufacture of said product; or
- (2) A product and a process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
- (4) A process and an apparatus or means specifically designed for carrying out the said process; or
- (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) above, unity of invention might not be present. Furthermore, the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art. The determination is made based on the contents of the claims as interpreted in light of the description and drawings. In the instant application, Groups \*\*\* have differing special technical features:

Group 1 has the special technical feature of binding proteins of a sample to a detectable affinity reagent and then applying the sample to an array of immobilized protein capture agents.

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Group 2 has the special technical feature of applying the sample to an array of immobilized protein capture agents and then binding proteins of a sample to a detectable affinity reagent.

Group 3 has the special technical feature a kit comprising an array, a buffer medium, and an affinity reagent.

Furthermore, the apparatus of group 3 has been taught by Wagner et al [US 6,329,209].